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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/606,763

06/29/2000

Hui Chen

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EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 07/16/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/606,763

Applicant(s)

CHEN ET AL.

Examiner

Chih-Min Kam

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-89 is/are pending in the application.
- 4a) Of the above claim(s) 8-11, 14-16, 18, 20-36 and 43-89 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 12 and 13 is/are allowed.
- 6) ☒ Claim(s) 1-7, 17, 19 and 37-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Claims 1-89 are pending.

Applicants' amendment filed on April 26, 2002 (Paper No. 12) is acknowledged, and applicants' response has been fully considered. Claims 1-7, 12, 13, 17, 19, 37, 39 and 41 have been amended, and claims 8-11, 14-16, 18, 20-36 and 43-89 are non-elected claims, thus withdrawn from consideration. Claims 1-7, 12, 13, 17, 19 and 37-42 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1-7, 12-13, 17, 19 and 37-42 under 35 U.S.C. 112 second paragraph, regarding the term "hCOMP", "COMP", "introducing DNA encoding hCOMP into cells", "at least", "bands of 50 kDa or 55 kDa" or "bands of 62 kDa or 67 kDa", "a differentiation agent" or lacking essential steps in preparing purified hCOMP, is withdrawn in view of applicants' amendment to the claims, applicants' response at pages 4-8 in Paper No. 13.

Claim Rejections - 35 USC § 103

3. The previous rejection of claim 37 under 35 U.S.C. 103(a) as being unpatentable over Heinegard *et al.* (WO 98/46253) taken with Junginger *et al.* (U. S. Patent 4,666,702), is withdrawn in view of applicants' response at pages 10-11 in Paper No. 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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4. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite because it depends from a non-elected claim, claim 8.

5. Claims 37-42 are indefinite because of the use of the term “type I collagen gel and type II collagen gel and purified cartilage oligomeric matrix protein”. The term “type I collagen gel and type II collagen gel and purified cartilage oligomeric matrix protein” renders the claim indefinite, it is unclear whether the material is type I collagen gel, type II collagen gel, purified cartilage oligomeric matrix protein, or the mixture of type I collagen gel, type II collagen gel and purified cartilage oligomeric matrix protein; it is also unclear whether the composition also contains the purified cartilage oligomeric matrix protein as the material of the biological matrix besides as the main ingredient. Claims 38-42 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 2, 4, 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hecht *et al.* (Matrix Biology 17, 269-278 (1998)) taken with Lawler *et al.* (J. Biol. Chem. 258, 12098-12101 (1983)) and DiCesare *et al.* (Eur. J. Biochem. 223, 927-937 (1994)).

Hecht *et al.* teach a full length human cartilage oligomeric matrix protein (hCOMP) is expressed in baculovirus system using pFASTBAC1 plasmid, and SF9 cells are used to generate the viruses. Pass 2 viruses in SF900II serum-free medium are used to produce recombinant proteins (page 271, right column-page 272 left column; claim 1, steps a and b; claim 7).

However, Hecht *et al.* do not indicate the purification of the protein. Lawler *et al.* teach that in the presence of calcium, thrombospondin is less asymmetric and comprises 3 or 4 nodular domains connected by thin flexible regions, however, the treatment of thrombospondin with EDTA results in partial denaturation of the nodular domains and an increased sensitivity to proteolysis by trypsin (page 12098, right column); and the reference further teaches a thrombospondin is purified by a heparin-Sepharose 4B column and the elution is carried out in the presence of 2 mM CaCl₂ (page 12098, right column, paragraph 4; claim 1, step c; claims 2, 4, 5). DiCesare *et al.* teach thrombospondin-1 (TSP-1), like COMP, is a non-collagenase matrix glycoprotein, COMP and TSP-1 have similarities in structure as demonstrated by molecular electron microscope, and both proteins have marked similarity at the C-terminus, including the calcium-binding type III domains (the paragraph bridges pages 927 and 928). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to express the

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hCOMP taught by Hecht *et al.* and to purify the protein in the same manner as TSP-1 taught by Lawler *et al.* because both proteins are structurally similar and have similar calcium binding domains as indicated by DiCesare *et al.*, furthermore, in the presence of calcium, hCOMP, like TSP-1 can be obtained as the native structure. Thus, the combined references result in the claimed invention and was, as a whole, *prima facie* obvious at the time the claimed invention was made.

In response, applicants indicate Hecht *et al.* teach the expression of hCOMP, but do not teach the purification of hCOMP in the presence of calcium; Lawler *et al.* teach the isolation of TSP-1 from platelet cells, but do not teach COMP and the purification of COMP from COMP-expression cells. Applicants further assert that since the purification method of COMP is known in the art (DiCesare *et al.*, 1994; Morgelin *et al.*, 1992), it is no reason to alter the known purification procedure to purify the recombinant hCOMP using a different method, e.g., the addition of calcium in the purification procedure as suggested in the combination of Hecht *et al.* and Lawler *et al.* The argument is not persuasive because the known purification method uses extraction with EDTA-containing buffer, while Lawler's method indicates the purification is carried out in the presence of calcium because the treatment of thrombospondin with EDTA results in the partial denaturation, thus, the advantage of using Lawler's method is to avoid protein denaturation. Regarding using Lawler's method to purify hCOMP, as discussed above, COMP and TSP-1 belong to the same thrombospondin gene family and have similarities in structure, and both proteins have the calcium-binding domains, thus it is obvious to use the combined references to obtain the purified hCOMP, wherein the preparation of the protein is recited in the claims.

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7. Claims 3, 6 and 17 are rejected because they depend from a rejected claim.

Conclusion

8. Claims 1-7, 17, 19 and 37-42 are rejected. It appears claims 12 and 13 are free of prior art and are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. *CMK*
Patent Examiner

Karen Cochrane Carlson PhD
KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER

July 3, 2002